Synopsis

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Title of thesis: "TO STUDY THE IMPACT OF EMF RADIATION FROM MOBILE HANDSETS ON CENTRAL GLUCOSENSING MECHANISMS AND MITOCHONDRIAL DYSFUNCTION IN FRUCTOSE FED DEVELOPING RATS"

Abstract

Introduction: The two scrooges in the lifestyle of modern day children/adolescents are exposure to electromagnetic radiations (EMF) from mobile phone and unrestricted intake of fructose rich diet from processed foods like beverages, confectionaries, pastries, cakes, soda etc. Simultaneously there has been an increase in the global incidence of insulin resistance and obesity amongst children-adolescents that were till now, the bane of adulthood (**Hu FB and Malik, 2010; Hardell, 2017**).

There is severe paucity of data to substantiate the available epidemiological data and correlate, exposure to EMF from the mobile phone and unrestricted fructose intake during pre, peri and post-pubertal stages with the development insulin resistance by early adulthood.

In order to address this lacuna, the present experimental study was designed with the objective to delineate the combined effects of EMF radiation from mobile handsets and fructose-rich diet on the central glucosensing mechanism, hepatic insulin resistance and mitochondrial dysfunction in developing age groups.

Methodology: Weaned male albino rats (4 weeks old) were randomly divided into four groups (n=6 each) – 'Normal', 'Exposure Only (ExpO)', 'Fructose Only (FruO)' and 'Exposure with Fructose (EF)'. The study spanned over 8 weeks, starting from the day of weaning of animals (age=28 day old) upto early adulthood (age=84 day old) to mark the pre, peri and post-pubertal stages of the lifetime of the animals. In addition to unrestricted access to standard laboratory chow, the control groups- Normal and FruO, were provided with filtered drinking water and fructose (15%) drinking solution, respectively. Parallel treatment groups-ExpO and EF were exposed to EMF radiations from mobile handsets (1760 MHz, 0.3988 mW/cm^2, GSM, specific absorption rate 0.181 W/kg, 2 h/d x 8 weeks) besides unrestricted access to standard laboratory chow with filtered drinking water or fructose

drinking solution (15%), respectively. The animals were assessed daily (food intake, water/fructose intake, body weight), and at the end of the study (hepatic and hypothalamic activity of enzymes of glycolysis and gluconeogenesis and expression of orexigenic (NPY, Ghrelin) and anorexigenic (POMC, Leptin) peptides, glucose transporter (GLUT 2)), expression of AMPK, SIRT-1, FOXO-1, insulin resistance markers, UCP2, OXPHOS, Oxidative stress markers and activity of the OXPHOS complex and SOD, catalase, GSH.

Results: The total calories consumed by the EF were higher by early adulthood than Normal, possibly under the influence of the raised levels of the orexigenic hormone i.e., ghrelin, and it reflected as raised rate of weight gain. At early adulthood, the response and sensitivity of insulin was significantly reduced ($p<0.05$) in EF *vs.* Normal. The hypothalamic and hepatic activity of the enzymes of glycolysis (hexokinase, phosphofructokinase) was significantly ($p<0.05$) reduced restrained but that of gluconeogenesis (lactate dehydrogenase, phosphoenolpyruvate carboxykinase, Fructose1,6-bisphosphatase and Glucose 6-Phosphatase) was raised. The lipid profile (triglyceride, total cholesterol, uric acid, AST, and ALT) and the glycogen levels were significantly ($p<0.05$) raised in EF *vs.* Normal. The hypothalamic protein expression of Orexigenic neuropeptide (NPY) was significantly ($p<0.05$) reduced in EF *vs.* Normal. The hypothalamic and hepatic protein expression of glucose transporter (GLUT 2) and glucokinase were significantly ($p<0.05$) reduced EF *vs.* Normal. The hypothalamic and hepatic protein expression of insulin resistance markers; IRS-1, p-PI3K, p-AKT were significantly ($p<0.05$) reduced EF *vs.* Normal. The hypothalamic and hepatic protein expression of master metabolic regulators; AMPK, p-AMPK, SIRT-1 and FOXO-1 were significantly ($p<0.05$) reduced EF *vs.* Normal. The protein expression and activity of oxidative phosphorylation in hypothalamus and hepatic were significantly ($p<0.05$) reduced EF *vs.* Normal; complex I, complex II, complex III, complex IV, complex V. The hypothalamic and hepatic protein expression of UCP2, MnSOD, catalase were significantly ($p<0.05$) reduced EF *vs.* Normal. The hypothalamic and hepatic activity of SOD2, catalase, glutathione reductase (GSH) were significantly ($p<0.05$) reduced EF *vs.* Normal.

Conclusions: The energy homeostasis of the EF was compromised as evidenced by **a)** reduced expression of the glycosensors-GLUT2 and glucokinase in the hypothalamus and liver **b)** reduced expression of the, orexigenic peptide–NPY and anorexigenic peptide-POMC in the hypothalamus by early adulthood. In EF, impaired master metabolic regulators perturbed the signals of oxidative phosphorylation and insulin functions as evidenced by **a)** reduced expression of the master metabolic regulators-AMPK, SIRT1 and FOXO1 in the

hypothalamus and liver **b)** reduced expression and activity of OXPHOS complex **c)** reduced expression and activity of antioxidative defence system i.e., SOD, catalase, GSH in the hypothalamus and liver. All of the data taken together perceive to incite the genesis of insulin resistance by early adulthood.

Outcomes of the overall work done: The outcomes of the concomitant effect of EMF radiation from mobile phone with 15% fructose drinking severely disturbed the pathways of eating and satiety behaviours that operate to maintain the "set-point" of energy homeostasis in hypothalamus and liver and further disturbed master metabolic regulator perturbed the signalling of mitochondrial OXPHOS and insulin function via alter PI3K/AKT pathway to initiate the genesis of insulin resistance and early onset of obesity by early adulthood.

Signature of Student **Signature of Supervisor(s)**